(FILE 'HOME' ENTERED AT 10:57:10 ON 04 OCT 2002)

FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE' ENTERED AT 10:57:22 ON 04 OCT 2002

L1	1022	FIBROBLAST GROWTH FACTOR RECEPTOR 2
L2	390	KERATINOCYTE GROWTH FACTOR RECEPTOR
L3	326	KGFR
L4	592	BEK
L5	0	PROTEIN TYROSINE KINASE 14
L6	0	PROTEIN TYROSINE KINASE 25
L8	226	K-
L9	75	JWS
L10	25	CEK3
L11	15	ECT1
L12	9	TK14
L13	10	TK25
L14	218	FGF RECEPTOR 2
L15	1262	FGFR2
L16	397	PFEIFFER SYNDROME
L17	2083	CRANIOFACIAL DYSOSTOSIS
L18	8	CFD-1
L19	978	CROUZON SYNDROME
L20	75507	ANTISENS?
L21	14845	RIBOZYM?
L22	15	L1 AND L20
L23	7	DUP REM L22 (8 DUPLICATES REMOVED)
L24	1	L1 AND L21
L25	8	L2 AND L20
L26	3	DUP REM L25 (5 DUPLICATES REMOVED)
L27	0	L2 AND L21
L28	4	L3 AND L20
L29	1	DUP REM L28 (3 DUPLICATES REMOVED)
L30	0	L3 AND L21
L31	5	L4 AND L20
L32	2	DUP REM L31 (3 DUPLICATES REMOVED)
L33	1	L4 AND L21
L34	226	K-
L35	2	L34 AND L20
L36	2	DUP REM L35 (0 DUPLICATES REMOVED)
L37	0	L9 AND L20
L38	0	L9 AND L21
L39	0	L10 AND L20
L40	0	L10 AND L21
L41	0	L11 AND L20
L42	0	L11 AND L21
L43	0	L12 AND L20
L44	0	L12 AND L21
L45	0	L13 AND L20
L46	0	L13 AND L21
L47	3	L14 AND L20
L48	3	DUP REM L47 (0 DUPLICATES REMOVED)
L49	0	L14 AND L21
L50	19	L15 AND L20
L51	9	DUP REM L50 (10 DUPLICATES REMOVED)
L52	0	L15 AND L21
L53	0	L16 AND L20
L54	0	L16 AND L21
L55	0	L17 AND L20
L56	0	L17 AND L21
L57	0	L18 AND L20
L58	0	L18 AND L21
L59	0	L19 AND L20
L60	0	L19 AND L21

L23 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 2002:214221 BIOSIS
DOCUMENT NUMBER: PREV200200214221
TITLE: Identification of Sef, a novel modulator of FGF signalling.
AUTHOR(S): Tsang, Michael; Friesel, Robert; Kudoh, Tetsuhiro; Dawid, Igor B. (1)
CORPORATE SOURCE: (1) Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892: idawid@nih.gov USA
SOURCE: Nature Cell Biology, (February, 2002) Vol. 4, No. 2, pp. 165-169. http://www.nature.com/ncb/. print.
ISSN: 1465-7392.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Fibroblast growth factors (FGFs) are members of a family of some 30 secreted proteins important in the regulation of cellular proliferation, migration, differentiation and survival. Here we report the identification of a novel modulator of FGF signal transduction, sef, isolated from a zebrafish embryo library through an in situ hybridization screen. The sef gene encodes a transmembrane protein, and belongs to the synexpression group that includes some of the fgf genes. Sef expression is positively regulated by FGF, and ectopic expression of sef in zebrafish or Xenopus laevis embryos specifically inhibits FGF signalling. In co-immunoprecipitation assays, the intracellular domain of Sef interacts with FGF receptors. FGFR1 and FGFR2. Injection of **antisense** sef morpholino oligos mimicked the phenotypes observed by ectopic fgf8 expression, suggesting that Sef is required to limit FGF signalling during development.

L23 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
ACCESSION NUMBER: 2001:257191 BIOSIS
DOCUMENT NUMBER: PREV200100257191
TITLE: Role of N-cadherin and protein kinase C in osteoblast gene activation induced by the S252W **fibroblast growth factor receptor 2** mutation in apert craniosynostosis.
AUTHOR(S): Lemonnier, Jerome; Hay, Eric; Delannoy, Philippe; Lomri, Abderrahim; Modrowski, Dominique; Caverzasio, Joseph; Marie, Pierre J. (1)
CORPORATE SOURCE: (1) Lariboisiere Hospital, Institut National de la Sante et de la Recherche Medicale, 2 rue Ambroise Pare, U 349, 75475, Paris Cedex, 10 France
SOURCE: Journal of Bone and Mineral Research, (May, 2001) Vol. 16, No. 5, pp. 832-845. print.
ISSN: 0884-0431.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Apert (Ap) syndrome is characterized by premature cranial suture ossification caused by **fibroblast growth factor receptor 2** (FGFR-2) mutations. We studied the role of cadherins and signaling events in the phenotypic alterations induced by the Ap FGFR-2 S252W mutation in mutant immortalized fetal human calvaria osteoblasts. The FGFR-2 mutation caused increased expression of the osteoblast markers alkaline phosphatase (ALP), type 1 collagen (COLIA1), and osteocalcin (OC) in long-term culture. The mutation also increased cell-cell aggregation, which was suppressed by specific neutralizing anti-N- and anti-E-cadherin antibodies. Mutant osteoblasts showed increased N- and E-cadherin, but not N-cell adhesion molecule (N-CAM) messenger RNA (mRNA) and protein levels. This was confirmed in vivo by the abundant immunoreactive N- and E-cadherins in preosteoblasts in the Ap suture whereas N-CAM and alpha- and beta-catenins were unaffected. Neutralizing anti-N-cadherin antibody or N-cadherin **antisense** (AS) oligonucleotides but not anti-E-cadherin antibody

or AS reduced ALP activity as well as ALP, COLIA1, and OC mRNA overexpression in mutant osteoblasts. Analysis of signal transduction revealed increased phospholipase Cgamma (PLCgamma) and protein kinase Calpha (PKCalpha) phosphorylation and increased PKC activity in mutant cells in basal conditions. Inhibition of PKC by calphostin C or the PKCalpha-specific inhibitor Go6976 suppressed the increased N-cadherin mRNA and protein levels as well as the overexpression of ALP, COLIA1, and OC mRNA in mutant cells. Thus, N-cadherin plays a role in the activation of osteoblast differentiation marker genes in mutant osteoblasts and PKCalpha signaling appears to be involved in the increased N-cadherin and osteoblast gene expression induced by the S252W FGFR-2 mutation in human osteoblasts.

L23 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
ACCESSION NUMBER: 1996:568693 BIOSIS
DOCUMENT NUMBER: PREV199799298049
TITLE: Keratinocyte growth factor and its receptor are involved in regulating early lung branching.
AUTHOR(S): Post, Martin (1); Souza, Patricia; Liu, Jason; Tseu, Irene; Wang, Jinxia; Kuliszewski, Maciej; Tanswell, A. Keith
CORPORATE SOURCE: (1) Med. Res. Council Group Lung Dev., Neonatal Res. Div., Dep. Pediatr., Hosp. Sick Child. Res. Inst., Univ. Toronto, Toronto, ON Canada
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3107-3115.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Lung branching morphogenesis depends on mesenchymal epithelial tissue interactions. Keratinocyte growth factor (KGF) has been implicated to be a regulator of these tissue interactions. In the present study, we investigated the role of KGF in early rat lung organogenesis. Reverse transcriptase-polymerase chain reaction analysis revealed KGF mRNA expression in the mesenchymal component of the 13-day embryonic lung, while message for KGF receptor (KGFR) was expressed in the epithelium, confirming the paracrine nature of KGF/KGFR axis. **Antisense** KGF oligonucleotides inhibited DNA synthesis of embryonic lung explants. This inhibitory effect of **antisense** KGF was partially reversed by the addition of exogenous KGF. Recombinant KGF was mitogenic for 13-day isolated embryonic lung epithelial cells. Medium conditioned by 13-day lung mesenchymal cells also stimulated DNA synthesis of 13-day embryonic lung epithelial cells. This stimulatory effect was partially abrogated by a neutralizing KGF antibody. The number of terminal buds of lung explants cultured in the presence of **antisense** KGF oligonucleotides was significantly reduced compared to control explants. Exogenous KGF partially abrogated the inhibitory effect of **antisense** KGF on early lung branching. Sense or scrambled KGF oligonucleotides had no inhibitory effect on lung growth and branching. Addition of neutralizing KGF antibodies to the explants also reduced the degree of branching, while non-immune IgG and neutralizing acidic FGF antibodies had no effect. Explants incubated with **antisense** oligonucleotides targeted to the initiation site of translation of both the splice variants of the **fibroblast growth factor receptor-2** (FGFR2) gene, KGFR and bek, exhibited a similar reduction in lung branching as observed with **antisense** KGF oligonucleotides. **Antisense** KGFR-specific oligonucleotides dramatically inhibited lung branching, while exposure of explants to **antisense** bek-specific oligonucleotides resulted in reduced branching albeit to a lesser degree than that observed with **antisense** KGFR-specific oligonucleotides. Neither sense nor scrambled KGFR-specific oligonucleotides had any effect on early lung branching. These results suggest that the KGF/KGFR system has a critical role in early lung organogenesis.

L23 ANSWER 4 OF 7 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999272682 MEDLINE
DOCUMENT NUMBER: 99272682 PubMed ID: 10339576
TITLE: Signaling through fibroblast growth factor receptor 2b plays a key role in the development of the exocrine pancreas.
AUTHOR: Miralles F; Czernichow P; Ozaki K; Itoh N; Scharfmann R
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale U457, Hospital R. Debre, 48, Boulevard Serurier, 75019 Paris, France.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 May 25) 96 (11) 6267-72. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 20000303
Entered Medline: 19990624

AB The development of the pancreas depends on epithelial-mesenchymal interactions. Fibroblast growth factors (FGFs) and their receptors (FGFRs 1-4) have been identified as mediators of epithelial-mesenchymal interactions in different organs. We show here that FGFR-2 IIIb and its ligands FGF-1, FGF-7, and FGF-10 are expressed throughout pancreatic development. We also show that in mesenchyme-free cultures of embryonic pancreatic epithelium FGF-1, FGF-7, and FGF-10 stimulate the growth, morphogenesis, and cytodifferentiation of the exocrine cells of the pancreas. The role of FGFs signaling through FGFR-2 IIIb was further investigated by inhibiting FGFR-2 IIIb signaling in organocultures of pancreatic explants (epithelium + mesenchyme) by using either **antisense** FGFR-2 IIIb oligonucleotides or a soluble recombinant FGFR-2 IIIb protein. Abrogation of FGFR-2 IIIb signaling resulted in a considerable reduction in the size of the explants and in a 2-fold reduction of the development of the exocrine cells. These results demonstrate that FGFs signaling through FGFR-2 IIIb play an important role in the development of the exocrine pancreas.

L23 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:219995 CAPLUS
DOCUMENT NUMBER: 130:306599
TITLE: Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913886	A1	19990325	WO 1998-US19419	19980917

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2304312	AA	19990325	CA 1998-2304312		19980917
AU 9893951	A1	19990405	AU 1998-93951		19980917
EP 1019065	A1	20000719	EP 1998-947089		19980917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
BR 9812650	A	20000822	BR 1998-12650		19980917
PRIORITY APPLN. INFO.:			US 1997-59160P	P	19970917
			US 1998-93972	A	19980609
			WO 1998-US19419	W	19980917

AB Antisense oligonucleotides carrying sequences that will allow them to bind to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs. Thus, phosphorothioate antisense oligonucleotide (HAdA1AS, 5'-gatggagggcggcatggcggg-3') designed for the adenosine A1 receptor is provided. HAdA1AS significantly and specifically reduces the in vivo response to adenosine challenge in a dose-dependent manner, is effective in protection against aeroallergen-induced bronchoconstriction (house dust mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition assocd. with lung airway, such as bronchoconstriction, inflammation, or allergies.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002157349 EMBASE

TITLE: Low-molecular-weight protein tyrosine phosphatase is a positive component of the fibroblast growth factor receptor signaling pathway.

AUTHOR: Park E.K.; Warner N.; Mood K.; Pawson T.; Daar I.O.

CORPORATE SOURCE: I.O. Daar, Building 560, National Cancer Institute-Frederick, Frederick, MD 21702, United States. daar@ncifcrf.gov

SOURCE: Molecular and Cellular Biology, (2002) 22/10 (3404-3414). Refs: 89
ISSN: 0270-7306 CODEN: MCEBD4

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Low-molecular-weight protein tyrosine phosphatase (LMW-PTP) has been implicated in the regulation of cell growth and actin rearrangement mediated by several receptor tyrosine kinases, including platelet-derived growth factor and epidermal growth factor. Here we identify the Xenopus laevis homolog of LMW-PTP1 (XLPTP1) as an additional positive regulator in the fibroblast growth factor (FGF) signaling pathway during Xenopus development. XLPTP1 has an expression pattern that displays substantial overlap with FGF receptor 1 (FGFR1) during Xenopus development. Using morpholino **antisense** technology, we show that inhibition of endogenous XLPTP1 expression dramatically restricts anterior and posterior structure development and inhibits mesoderm formation. In ectodermal explants, loss of XLPTP1 expression dramatically blocks the induction of the early mesoderm gene, Xbrachyury (Xbra), by FGF and partially blocks Xbra induction by Activin. Moreover, FGF-induced activation of mitogen-activated protein (MAP) kinase is also inhibited by XLPTP1 morpholino **antisense** oligonucleotides; however, introduction of RNA encoding XLPTP1 is able to rescue morphological and biochemical

effects of **antisense** inhibition. Inhibition of FGF-induced MAP kinase activity due to loss of XLPTP1 is also rescued by an active Ras, implying that XLPTP1 may act upstream of or parallel to Ras. Finally, XLPTP1 physically associates only with an activated FGFR1, and this interaction requires the presence of SNT1/FRS-2 (FGFR substrate 2). Although LMW-PTP1 has been shown to participate in other receptor systems, the data presented here also reveal XLPTP1 as a new and important component of the FGF signaling pathway.

L23 ANSWER 7 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002219691 EMBASE
TITLE: Control of alternative splicing by **antisense** oligonucleotides as a potential chemotherapy: Effects on gene expression.
AUTHOR: Mercatante D.R.; Kole R.
CORPORATE SOURCE: R. Kole, Department of Pharmacology, Lineberger Compreh. Cancer Center, University of North Carolina, Chapel Hill, NC 27599, United States. kole@med.unc.edu
SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease, (18 Jul 2002) 1587/2-3 (126-132).
Refs: 94
ISSN: 0925-4439 CODEN: BBADEX
PUBLISHER IDENT.: S 0925-4439(02)00075-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Expression of alternatively spliced mRNA variants at specific stages of development or in specific cells and tissues contributes to the functional diversity of the human genome. Aberrations in alternative splicing were found as a cause or a contributing factor to the development, progression, or maintenance of various diseases including cancer. The use of **antisense** oligonucleotides to modify aberrant expression patterns of alternatively spliced mRNAs is a novel means of potentially controlling such diseases. However, to utilize **antisense** oligonucleotides as molecular chemotherapeutic agents, the global effects of these molecules need to be examined. The advent of gene expression array technology has now made it possible to simultaneously examine changes that occur in the expression levels of several thousand genes in response to **antisense** treatment. This analysis should help in the development of more specific and efficacious **antisense** oligonucleotides as molecular therapeutics. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L24 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:171789 CAPLUS
DOCUMENT NUMBER: 124:250933
TITLE: Ribozymes cleaving growth factor mRNAs for treatment of restenosis and cancers
INVENTOR(S): Stinchcomb, Dan T.; Draper, Kenneth; McSwiggen, James; Jarvis, Thale
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 32
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531541	A2	19951123	WO 1995-US6368	19950518
WO 9531541	A3	19960425		
W: AU, CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5646042	A	19970708	US 1995-373124	19950113
US 5817796	A	19981006	US 1995-435628	19950505
AU 9526422	A1	19951205	AU 1995-26422	19950518
EP 763106	A1	19970319	EP 1995-921311	19950518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10500309	T2	19980113	JP 1995-529908	19950518
US 6103890	A	20000815	US 1997-998099	19971224
AU 9851819	A1	19980611	AU 1998-51819	19980112
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713

PRIORITY APPLN. INFO.:

US 1994-245466	A	19940518
US 1995-373124	A	19950113
US 1992-936422	B1	19920826
US 1992-987132	B2	19921207
US 1994-192943	A2	19940207
AU 1995-26422	A3	19950518
WO 1995-US6368	W	19950518
US 1996-623891	A	19960325
US 1997-37658P	P	19970123

AB Ribozymes that cleave RNA precursors for proliferation factors and so that can be used to limit cell proliferation are described for use in the prevention of restenosis and in the treatment of cancers. Specifically, ribozymes effective against c-myb transcripts are described although ribozymes against other growth factors such as c-myc and c-fos may also be useful. The selection of hammerhead ribozyme cleavage sites in the c-myb mRNA and the screening and optimization of ribozyme activity are demonstrated. Tests in cell culture showed that effective ribozymes complexed with the cationic lipid Lipofectamine or a 1:1 mixt. of DMRE and DOPE were able to inhibit smooth muscle cell proliferation in a dose-dependent manner. Optimization expts. in which the effects of nucleotide and backbone substitution were studied to develop ribozymes for use in vivo are also reported. Delivery of the ribozyme to an injury site and successful inhibition of smooth muscle cell proliferation are demonstrated.

L26 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 2001:515240 BIOSIS
DOCUMENT NUMBER: PREV200100515240
TITLE: A role for the perlecan protein core in the activation of the **keratinocyte growth factor receptor**.
AUTHOR(S): Ghiselli, Giancarlo; Eichstetter, Inge; Iozzo, Renato V. (1)
CORPORATE SOURCE: (1) Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, 1020 Locust Street, Philadelphia, PA, 19107: iozzo@lac.jci.tju.edu USA
SOURCE: Biochemical Journal, (1 October, 2001) Vol. 359, No. 1, pp. 153-163. print.
ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Perlecan, a widespread heparan sulphate (HS) proteoglycan, is directly involved in the storing of angiogenic growth factors, mostly members of the fibroblast growth factor (FGF) gene family. We have previously shown that **antisense** targeting of the perlecan gene causes a reduced growth and responsiveness to FGF7 (also known as keratinocyte growth factor (KGF)) in human cancer cells, and that the perlecan protein core interacts specifically with FGF7. In the present paper, we have investigated human colon carcinoma cells in which the perlecan gene was disrupted by targeted homologous recombination. After screening over 1000 clones, we obtained two clones heterozygous for the null mutation with no detectable perlecan, indicating that the other allele was non-functioning. The perlecan-deficient cells grew more slowly, did not respond to FGF7 with or without the addition of heparin, and were less tumorigenic than control cells. Paradoxically, the perlecan-deficient cells displayed increased FGF7 surface binding. However, the perlecan protein core was required for functional activation of the KGF receptor and downstream signalling. Because heparin could not substitute for perlecan, the HS chains are not critical for FGF7-mediated signalling in this cell system. These results provide the first genetic evidence that the perlecan protein core is a molecular entity implicated in FGF7 binding and activation of its receptor.

L26 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
ACCESSION NUMBER: 1996:568693 BIOSIS
DOCUMENT NUMBER: PREV199799298049
TITLE: Keratinocyte growth factor and its receptor are involved in regulating early lung branching.
AUTHOR(S): Post, Martin (1); Souza, Patricia; Liu, Jason; Tseu, Irene; Wang, Jinxia; Kuliszewski, Maciej; Tanswell, A. Keith
CORPORATE SOURCE: (1) Med. Res. Council Group Lung Dev., Neonatal Res. Div., Dep. Pediatr., Hosp. Sick Child. Res. Inst., Univ. Toronto, Toronto, ON Canada
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3107-3115.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Lung branching morphogenesis depends on mesenchymal epithelial tissue interactions. Keratinocyte growth factor (KGF) has been implicated to be a regulator of these tissue interactions. In the present study, we investigated the role of KGF in early rat lung organogenesis. Reverse transcriptase-polymerase chain reaction analysis revealed KGF mRNA expression in the mesenchymal component of the 13-day embryonic lung, while message for KGF receptor (KGFR) was expressed in the epithelium, confirming the paracrine nature of KGF/KGFR axis. **Antisense** KGF oligonucleotides inhibited DNA synthesis of embryonic lung explants. This inhibitory effect of **antisense** KGF was partially reversed by the

addition of exogenous KGF. Recombinant KGF was mitogenic for 13-day isolated embryonic lung epithelial cells. Medium conditioned by 13-day lung mesenchymal cells also stimulated DNA synthesis of 13-day embryonic lung epithelial cells. This stimulatory effect was partially abrogated by a neutralizing KGF antibody. The number of terminal buds of lung explants cultured in the presence of **antisense** KGF oligonucleotides was significantly reduced compared to control explants. Exogenous KGF partially abrogated the inhibitory effect of **antisense** KGF on early lung branching. Sense or scrambled KGF oligonucleotides had no inhibitory effect on lung growth and branching. Addition of neutralizing KGF antibodies to the explants also reduced the degree of branching, while non-immune IgG and neutralizing acidic FGF antibodies had no effect. Explants incubated with **antisense** oligonucleotides targeted to the initiation site of translation of both the splice variants of the fibroblast growth factor receptor-2 (FGFR2) gene, KGFR and bek, exhibited a similar reduction in lung branching as observed with **antisense** KGF oligonucleotides. **Antisense** KGFR-specific oligonucleotides dramatically inhibited lung branching, while exposure of explants to **antisense** bek-specific oligonucleotides resulted in reduced branching albeit to a lesser degree than that observed with **antisense** KGFR-specific oligonucleotides. Neither sense nor scrambled KGFR-specific oligonucleotides had any effect on early lung branching. These results suggest that the KGF/KGFR system has a critical role in early lung organogenesis.

L26 ANSWER 3 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96277266 EMBASE
DOCUMENT NUMBER: 1996277266
TITLE: Keratinocyte growth factor and receptor mRNA expression in benign and malignant human prostate.
AUTHOR: McGarvey T.W.; Stearns M.E.
CORPORATE SOURCE: Department of Pathology, Allegheny Univ. of Health Sciences, Broad and Vine Sts.,Philadelphia, PA 19102-1192, United States
SOURCE: Experimental and Molecular Pathology, (1995) 63/1 (52-62). ISSN: 0014-4800 CODEN: EXMPA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have examined whether keratinocyte growth factor (KGF) and its receptor are expressed in normal, fetal, and prostate cancer cells since KGF may play a role in the growth of adenocarcinomas. In situ hybridization studies with digoxigenin-labeled oligonucleotides (anti-sense and sense controls) were employed to examine KGF and KGF receptor mRNA expression in prostate cancer. We found that the KGF and KGF receptor genes were faintly expressed in the stromal and epithelial cells, respectively, in both fetal (n = 6) and normal adult prostate (n = 6) tissues examined. In 10 benign prostatic hyperplasias (BPH), and in low- and high-grade prostatic carcinoma (32 total), both the KGF gene and the receptor mRNA were expressed in the glandular epithelial cells. KGF was also expressed by the stromal cells in BPH and low-grade carcinoma. Computer assisted system analysis indicated that the intensity of epithelial labeling by both probes was increased in high Gleason score carcinomas (>8) and in metastatic nodules. We interpret the data to mean that the paracrine loop in normal prostate may be replaced by an autocrine loop in BPH and adenocarcinomas.

L29 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 1996:568693 BIOSIS
DOCUMENT NUMBER: PREV199799298049
TITLE: Keratinocyte growth factor and its receptor are involved in regulating early lung branching.
AUTHOR(S): Post, Martin (1); Souza, Patricia; Liu, Jason; Tseu, Irene; Wang, Jinxia; Kuliszewski, Maciej; Tanswell, A. Keith
CORPORATE SOURCE: (1) Med. Res. Council Group Lung Dev., Neonatal Res. Div., Dep. Pediatr., Hosp. Sick Child. Res. Inst., Univ. Toronto, Toronto, ON Canada
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3107-3115.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Lung branching morphogenesis depends on mesenchymal epithelial tissue interactions. Keratinocyte growth factor (KGF) has been implicated to be a regulator of these tissue interactions. In the present study, we investigated the role of KGF in early rat lung organogenesis. Reverse transcriptase-polymerase chain reaction analysis revealed KGF mRNA expression in the mesenchymal component of the 13-day embryonic lung, while message for KGF receptor (**KGFR**) was expressed in the epithelium, confirming the paracrine nature of KGF/**KGFR** axis. **Antisense** KGF oligonucleotides inhibited DNA synthesis of embryonic lung explants. This inhibitory effect of **antisense** KGF was partially reversed by the addition of exogenous KGF. Recombinant KGF was mitogenic for 13-day isolated embryonic lung epithelial cells. Medium conditioned by 13-day lung mesenchymal cells also stimulated DNA synthesis of 13-day embryonic lung epithelial cells. This stimulatory effect was partially abrogated by a neutralizing KGF antibody. The number of terminal buds of lung explants cultured in the presence of **antisense** KGF oligonucleotides was significantly reduced compared to control explants. Exogenous KGF partially abrogated the inhibitory effect of **antisense** KGF on early lung branching. Sense or scrambled KGF oligonucleotides had no inhibitory effect on lung growth and branching. Addition of neutralizing KGF antibodies to the explants also reduced the degree of branching, while non-immune IgG and neutralizing acidic FGF antibodies had no effect. Explants incubated with **antisense** oligonucleotides targeted to the initiation site of translation of both the splice variants of the fibroblast growth factor receptor-2 (FGFR2) gene, **KGFR** and bek, exhibited a similar reduction in lung branching as observed with **antisense** KGF oligonucleotides. **Antisense KGFR**-specific oligonucleotides dramatically inhibited lung branching, while exposure of explants to **antisense** bek-specific oligonucleotides resulted in reduced branching albeit to a lesser degree than that observed with **antisense KGFR** -specific oligonucleotides. Neither sense nor scrambled **KGFR** -specific oligonucleotides had any effect on early lung branching. These results suggest that the KGF/**KGFR** system has a critical role in early lung organogenesis.

L32 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 1996:568693 BIOSIS
DOCUMENT NUMBER: PREV199799298049
TITLE: Keratinocyte growth factor and its receptor are involved in regulating early lung branching.
AUTHOR(S): Post, Martin (1); Souza, Patricia; Liu, Jason; Tseu, Irene; Wang, Jinxia; Kuliszewski, Maciej; Tanswell, A. Keith
CORPORATE SOURCE: (1) Med. Res. Council Group Lung Dev., Neonatal Res. Div., Dep. Pediatr., Hosp. Sick Child. Res. Inst., Univ. Toronto, Toronto, ON Canada
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3107-3115.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Lung branching morphogenesis depends on mesenchymal epithelial tissue interactions. Keratinocyte growth factor (KGF) has been implicated to be a regulator of these tissue interactions. In the present study, we investigated the role of KGF in early rat lung organogenesis. Reverse transcriptase-polymerase chain reaction analysis revealed KGF mRNA expression in the mesenchymal component of the 13-day embryonic lung, while message for KGF receptor (KGFR) was expressed in the epithelium, confirming the paracrine nature of KGF/KGFR axis. **Antisense** KGF oligonucleotides inhibited DNA synthesis of embryonic lung explants. This inhibitory effect of **antisense** KGF was partially reversed by the addition of exogenous KGF. Recombinant KGF was mitogenic for 13-day isolated embryonic lung epithelial cells. Medium conditioned by 13-day lung mesenchymal cells also stimulated DNA synthesis of 13-day embryonic lung epithelial cells. This stimulatory effect was partially abrogated by a neutralizing KGF antibody. The number of terminal buds of lung explants cultured in the presence of **antisense** KGF oligonucleotides was significantly reduced compared to control explants. Exogenous KGF partially abrogated the inhibitory effect of **antisense** KGF on early lung branching. Sense or scrambled KGF oligonucleotides had no inhibitory effect on lung growth and branching. Addition of neutralizing KGF antibodies to the explants also reduced the degree of branching, while non-immune IgG and neutralizing acidic FGF antibodies had no effect. Explants incubated with **antisense** oligonucleotides targeted to the initiation site of translation of both the splice variants of the fibroblast growth factor receptor-2 (FGFR2) gene, KGFR and **bek**, exhibited a similar reduction in lung branching as observed with **antisense** KGF oligonucleotides. **Antisense** KGFR-specific oligonucleotides dramatically inhibited lung branching, while exposure of explants to **antisense bek**-specific oligonucleotides resulted in reduced branching albeit to a lesser degree than that observed with **antisense** KGFR-specific oligonucleotides. Neither sense nor scrambled KGFR-specific oligonucleotides had any effect on early lung branching. These results suggest that the KGF/KGFR system has a critical role in early lung organogenesis.

L32 ANSWER 2 OF 2 MEDLINE
ACCESSION NUMBER: 95054295 MEDLINE
DOCUMENT NUMBER: 95054295 PubMed ID: 7964981
TITLE: Basic fibroblast growth factor and fibroblast growth factor receptor I are implicated in the growth of human astrocytomas.
AUTHOR: Morrison R S; Yamaguchi F; Saya H; Bruner J M; Yahanda A M; Donehower L A; Berger M
CORPORATE SOURCE: Department of Neurosurgery, University of Texas M.D. Anderson Cancer Center, Houston 77030.
SOURCE: JOURNAL OF NEURO-ONCOLOGY, (1994) 18 (3) 207-16. Ref: 74
Journal code: 8309335. ISSN: 0167-594X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941128

AB Malignant astrocytomas are highly invasive, vascular neoplasms that comprise the majority of nervous system tumors in humans. A strong association has previously been made between malignancy in human astrocytic tumors and increased expression of certain fibroblast growth factor (FGF) family members, including basic and acidic FGF. The influence of endogenous basic FGF on glioblastoma cell growth in vitro was evaluated using basic FGF-specific **antisense** oligonucleotides. These studies indicated that human glioblastoma cell growth in vitro, can be inhibited by suppressing basic FGF expression. Human astrocytomas also exhibited changes in FGF receptor (FGFR) expression during the course of their progression from a benign to a malignant phenotype. FGFR2 (**bek**) expression was abundant in normal white matter and in all low grade astrocytomas, but was not observed in glioblastomas. Conversely, FGFR1 (flg) expression was absent or barely detectable in normal white matter, but was significantly elevated in glioblastomas. Glioblastomas also expressed an alternatively spliced form of FGFR1 containing two immunoglobulin-like disulfide loops (FGFR1 beta), whereas normal human adult and fetal brain expressed a form of the receptor containing three immunoglobulin-like disulfide loops (FGFR1 alpha). Intermediate grades of astrocytic tumors exhibited a gradual loss of FGFR2 and a shift in expression from FGFR1 alpha to FGFR1 beta as they progressed from a benign to a malignant phenotype. The underlying cytogenetic changes that contribute to these alterations are not entirely understood, but abnormalities in the p53 tumor suppressor gene may influence expression of bFGF as well as the FGFR. These results suggest that alterations in FGFR signal transduction pathways may play a critical role in the malignant progression of astrocytic tumors.

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L33 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:554940 CAPLUS
DOCUMENT NUMBER: 125:189381
TITLE: Multiple component RNA catalysts and their use in targeted cleavage of mRNA
INVENTOR(S): Pyle, Anna M.; Michels, William J.
PATENT ASSIGNEE(S): Trustees of Columbia University in the City of New York, USA
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622689	A1	19960801	WO 1996-US1337	19960125
W: AU, CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5872241	A	19990216	US 1995-378235	19950125
AU 9649114	A1	19960814	AU 1996-49114	19960125

PRIORITY APPLN. INFO.: US 1995-378235 19950125
WO 1996-US1337 19960125

AB This invention is directed to a compn. for catalyzed oligonucleotide cleavage comprising a synthetic non-naturally occurring oligonucleotide compd. The compd. comprises nucleotides whose sequence defines a conserved group II intron catalytic region and nucleotides whose sequence is capable of hybridizing with a predetd. oligonucleotide target sequence to be cleaved, such target sequence not being present within the compd. The compn. also includes an appropriate oligonucleotide co-factor. Preferably, the conserved group II intron catalytic region is a group II intron domain I catalytic region. In one embodiment the conserved group II intron domain I catalytic region may further comprise a conserved portion of a group II intron domain II, a group II intron domain III, a group II intron domain IV, a group II intron domain V, or a group II intron domain VI. The invention is also directed to methods of treatment and methods of use of such compds. Sep. group II intron domains were combined to create enzymically active **ribozymes**. These **ribozymes** were examd. to det. kinetics and mechanism of substrate cleavage.

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L36 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:320060 CAPLUS
DOCUMENT NUMBER: 134:339179
TITLE: Nucleic acids and proteins associated with cancer as antitumor targets
INVENTOR(S): Burmer, Glenna C.; Brown, Joseph P.; Pritchard, David
PATENT ASSIGNEE(S): Lifespan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030964	A2	20010503	WO 2000-US29126	20001020
WO 2001030964	A3	20010809		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001013397	A5	20010508	AU 2001-13397	20001020

PRIORITY APPLN. INFO.: US 1999-161232P P 19991022
US 2000-693783 A 20001019
WO 2000-US29126 W 20001020

AB This invention relates to the discovery of nucleic acids assocd. with cell proliferation, neoplasia, cell transformation, malignant tumor formation and metastasis and uses therefor. The present invention provides a method for cancer diagnosing by detecting the overexpression or the underexpression of a cancer-assocd. mRNA in the tissue of interest, preferably in liver, breast, prostate, kidney and colon. In another aspect, the invention provides methods for arresting cancer and a method for identifying a modulators of cancer development.

L36 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:12588 CAPLUS
DOCUMENT NUMBER: 134:81772
TITLE: Stress-inducible GRP78 promoter and its use in gene therapy
INVENTOR(S): Lee, Amy S.
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000791	A1	20010104	WO 2000-US17885	20000628
WO 2001000791	C2	20020725		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1194527 A1 20020410 EP 2000-948536 20000628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-141505P P 19990628
WO 2000-US17885 W 20000628

AB This invention relates to compns. and methods for selective expression of a heterologous nucleic acid sequence in a targeted tissue, and more particularly to the glucose regulated protein 78 (grp78) stress-responsive promoter and its use in gene therapy and the prodn. of transgenic animals. Thus, a retroviral vector contg. a herpes simplex virus thymidine kinase gene controlled by the rat GRP78 promoter was prepd. In B/C10ME cells (mouse mammary adenocarcinoma cells) contg. this vector, expression of the thymidine kinase gene was induced by glucose deprivation. The recombinant B/C10ME cells were injected into mice. After tumors had developed, ganciclovir was admininistered. Tumor regression was obsd. in these mice, unlike those injected with unaltered B/C10ME cells.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 1 OF 3 MEDLINE
ACCESSION NUMBER: 2002159331 MEDLINE
DOCUMENT NUMBER: 21888504 PubMed ID: 11891984
TITLE: Region- and stage-specific effects of FGFs and BMPs in chick mandibular morphogenesis.
AUTHOR: Mina Mina; Wang Yu-Hsing; Ivanisevic Ana-Maria; Upholt William B; Rodgers Barbara
CORPORATE SOURCE: Department of Pediatric Dentistry, School of Dental Medicine, University of Connecticut Health Center, Farmington, CT 06030, USA.. mina@nsol.uchc.edu
CONTRACT NUMBER: DE 08682 (NIDCR)
SOURCE: DEVELOPMENTAL DYNAMICS, (2002 Mar) 223 (3) 333-52. Journal code: 9201927. ISSN: 1058-8388.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020314
Last Updated on STN: 20020618
Entered Medline: 20020617

AB The mandibular processes are specified as at least two independent functional regions: two large lateral regions where morphogenesis is dependent on fibroblast growth factor (FGF)-8 signaling, and a small medial region where morphogenesis is independent of FGF-8 signaling. To gain insight into signaling pathways that may be involved in morphogenesis of the medial region, we have examined the roles of pathways regulated by FGFs and bone morphogenetic proteins (BMPs) in morphogenesis of the medial and lateral regions of the developing chick mandible. Our results show that, unlike in the lateral region, the proliferation and growth of the mesenchyme in the medial region is dependent on signals derived from the overlying epithelium. We also show that medial and lateral mandibular mesenchyme respond differently to exogenous FGFs and BMPs. FGF-2 and FGF-4 can mimic many of the effects of mandibular epithelium from the medial region, including supporting the expression of Msx genes, outgrowth of the mandibular processes and elongation of Meckel's cartilage. On the other hand, laterally placed FGF beads did not induce ectopic expression of Msx genes and did not affect the growth of the mandibular processes. These functional studies, together with our tissue distribution studies, suggest that FGF-mediated signaling (other than FGF-8), through interactions with **FGF receptor-2** and downstream target genes including Msx genes, is part of the signaling pathway that mediates the growth-promoting interactions in the medial region of the developing mandible. Our observations also suggest that BMPs play multiple stage- and region-specific roles in mandibular morphogenesis. In this study, we show that exogenous BMP-7 applied to the lateral region at early stages of development (stage 20) caused apoptosis, ectopic expression of Msx genes, and inhibited outgrowth of the mandibular processes and the formation of Meckel's cartilage. Our additional experiments suggest that the differences between the effects of BMP-7 on lateral mandibular mesenchyme at stage 20 and previously reported results at stage 23 (Wang et al., [1999] Dev. Dyn. 216:320-335) are related to differences in stages of differentiation in that BMP-7 promotes apoptosis in undifferentiated lateral mandibular mesenchyme, whereas it promotes chondrogenesis at later stages of development. We also showed that, unlike mandibular epithelium and medially placed FGF beads, medially placed BMP-7 did not support outgrowth of the isolated mesenchyme and at stage 20 induced the formation of a duplicated rod of cartilage extending from the body of Meckel's cartilage. These observations suggest that BMPs do not play essential roles in growth-promoting interactions in the medial region of the developing mandible. However, BMP-mediated signaling is a part of the signaling pathways regulating chondrogenesis of the mandibular mesenchyme.

L48 ANSWER 2 OF 3 MEDLINE
ACCESSION NUMBER: 2002461850 IN-PROCESS
DOCUMENT NUMBER: 22209201 PubMed ID: 12221006
TITLE: Ectodermal FGFs Induce Perinodular Inhibition of Limb Chondrogenesis in Vitro and in Vivo via **FGF Receptor 2**.
AUTHOR: Moftah Marie; Downie Sherry; Bronstein Natalie; Mezentseva Nadezhda; Pu Jiayu; Maher Pamela; Newman Stuart
SOURCE: DEVELOPMENTAL BIOLOGY, (2002 Sep 15) 249 (2) 270. Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020911
Last Updated on STN: 20020911

AB The formation of cartilage elements in the developing vertebrate limb, where they serve as primordia for the appendicular skeleton, is preceded by the appearance of discrete cellular condensations. Control of the size and spacing of these condensations is a key aspect of skeletal pattern formation. Limb bud cell cultures grown in the absence of ectoderm formed continuous sheet-like masses of cartilage. With the inclusion of ectoderm, these cultures produced one or more cartilage nodules surrounded by zones of noncartilaginous mesenchyme. Ectodermal fibroblast growth factors (FGF2 and FGF8), but not a mesodermal FGF (FGF7), substituted for ectoderm in inhibiting chondrogenic gene expression, with some combinations of the two ectodermal factors leading to well-spaced cartilage nodules of relatively uniform size. Treatment of cultures with SU5402, an inhibitor FGF receptor tyrosine kinase activity, rendered FGFs ineffective in inducing perinodular inhibition. Inhibition of production of **FGF receptor 2** (FGFR2) by transfection of wing and leg cell cultures with **antisense** oligodeoxynucleotides blocked appearance of ectoderm- or FGF-induced zones of perinodular inhibition of chondrogenesis and, when introduced into the limb buds of developing embryos, led to shorter, thicker, and fused cartilage elements. Because FGFR2 is expressed mainly at sites of precartilage condensation during limb development in vivo and in vitro, these results suggest that activation of FGFR2 by FGFs during development elicits a lateral inhibitor of chondrogenesis that limits the expansion of developing skeletal elements.

L48 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:661781 CAPLUS
TITLE: Ectodermal FGFs Induce Perinodular Inhibition of Limb Chondrogenesis in Vitro and in Vivo via **FGF Receptor 2**
AUTHOR(S): Moftah, Marie Z.; Downie, Sherry A.; Bronstein, Natalie B.; Mezentseva, Nadezhda; Pu, Jiayu; Maher, Pamela A.; Newman, Stuart A.
CORPORATE SOURCE: Department of Cell Biology and Anatomy, New York Medical College, Valhalla, NY, 10595, USA
SOURCE: Developmental Biology (Orlando, FL, United States) (2002), 249(2), 270-282
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The formation of cartilage elements in the developing vertebrate limb, where they serve as primordia for the appendicular skeleton, is preceded by the appearance of discrete cellular condensations. Control of the size and spacing of these condensations is a key aspect of skeletal pattern formation. Limb bud cell cultures grown in the absence of ectoderm formed continuous sheet-like masses of cartilage. With the inclusion of ectoderm, these cultures produced one or more cartilage nodules surrounded

by zones of noncartilaginous mesenchyme. Ectodermal fibroblast growth factors (FGF2 and FGF8), but not a mesodermal FGF (FGF7), substituted for ectoderm in inhibiting chondrogenic gene expression, with some combinations of the two ectodermal factors leading to well-spaced cartilage nodules of relatively uniform size. Treatment of cultures with SU5402, an inhibitor FGF receptor tyrosine kinase activity, rendered FGFs ineffective in inducing perinodular inhibition. Inhibition of prodn. of **FGF receptor 2** (FGFR2) by transfection of wing and leg cell cultures with **antisense** oligodeoxynucleotides blocked appearance of ectoderm- or FGF-induced zones of perinodular inhibition of chondrogenesis and, when introduced into the limb buds of developing embryos, led to shorter, thicker, and fused cartilage elements. Because FGFR2 is expressed mainly at sites of precartilage condensation during limb development in vivo and in vitro, these results suggest that activation of FGFR2 by FGFs during development elicits a lateral inhibitor of chondrogenesis that limits the expansion of developing skeletal elements.

L51 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 2002:214221 BIOSIS
DOCUMENT NUMBER: PREV200200214221
TITLE: Identification of Sef, a novel modulator of FGF signalling.
AUTHOR(S): Tsang, Michael; Friesel, Robert; Kudoh, Tetsuhiro; Dawid, Igor B. (1)
CORPORATE SOURCE: (1) Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892: idawid@nih.gov USA
SOURCE: Nature Cell Biology, (February, 2002) Vol. 4, No. 2, pp. 165-169. http://www.nature.com/ncb/. print.
ISSN: 1465-7392.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Fibroblast growth factors (FGFs) are members of a family of some 30 secreted proteins important in the regulation of cellular proliferation, migration, differentiation and survival. Here we report the identification of a novel modulator of FGF signal transduction, sef, isolated from a zebrafish embryo library through an in situ hybridization screen. The sef gene encodes a transmembrane protein, and belongs to the synexpression group that includes some of the fgf genes. Sef expression is positively regulated by FGF, and ectopic expression of sef in zebrafish or Xenopus laevis embryos specifically inhibits FGF signalling. In co-immunoprecipitation assays, the intracellular domain of Sef interacts with FGF receptors. FGFR1 and **FGFR2**. Injection of **antisense** sef morpholino oligos mimicked the phenotypes observed by ectopic fgf8 expression, suggesting that Sef is required to limit FGF signalling during development.

L51 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
ACCESSION NUMBER: 2001:279355 BIOSIS
DOCUMENT NUMBER: PREV200100279355
TITLE: Evidence that SPROUTY2 functions as an inhibitor of mouse embryonic lung growth and morphogenesis.
AUTHOR(S): Mailleux, Arnaud Andre; Tefft, Denise; Ndiaye, Delphine; Itoh, Nobuyuki; Thiery, Jean Paul; Warburton, David; Bellusci, Saverio (1)
CORPORATE SOURCE: (1) UMR144-CNRS/Institut Curie, 26 Rue d'Ulm, 75248, Paris Cedex 05: saverio.bellusci@curie.fr France
SOURCE: Mechanisms of Development, (April, 2001) Vol. 102, No. 1-2, pp. 81-94. print.
ISSN: 0925-4773.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Experimental evidence is rapidly emerging that the coupling of positive regulatory signals with the induction of negative feedback modulators is a mechanism of fine regulation in development. Studies in Drosophila and chick have shown that members of the SPROUTY family are inducible negative regulators of growth factors that act through tyrosine kinase receptors. We and others have shown that Fibroblast Growth Factor 10 (FGF10) is a key positive regulator of lung branching morphogenesis. Herein, we provide direct evidence that mSprouty2 is dynamically expressed in the peripheral endoderm in embryonic lung and is downregulated in the clefts between new branches at E12.5. We found that mSprouty2 was expressed in a domain restricted in time and space, adjacent to that of Fgf10 in the peripheral mesenchyme. By E14.5, Fgf10 expression was restricted to a narrow domain of mesenchyme along the extreme edges of the individual lung lobes, whereas mSprouty2 was most highly expressed in the subjacent epithelial terminal buds. FGF10 beads upregulated the expression of mSprouty2 in adjacent epithelium in embryonic lung explant culture. Lung cultures treated with exogenous FGF10 showed greater branching and higher levels of mSpry2 mRNA. Conversely, Fgf10 **antisense** oligonucleotides reduced branching and decreased mSpry2 mRNA levels. However, treatment

with exogenous FGF10 or **antisense** Fgf10 did not change Shh and **FgfR2** mRNA levels in the lungs. We investigated Sprouty2 function during lung development by two different but complementary approaches. The targeted overexpression of mSprouty2 in the peripheral lung epithelium in vivo, using the Surfactant Protein C promoter, resulted in a low level of branching, lung lobe edges abnormal in appearance and the inhibition of epithelial proliferation. Transient high-level overexpression of mSpry2 throughout the pulmonary epithelium by intra-tracheal adenovirus microinjection also resulted in a low level of branching. These results indicate for the first time that mSPROUTY2 functions as a negative regulator of embryonic lung morphogenesis and growth.

L51 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1996:568693 BIOSIS
DOCUMENT NUMBER: PREV199799298049
TITLE: Keratinocyte growth factor and its receptor are involved in regulating early lung branching.
AUTHOR(S): Post, Martin (1); Souza, Patricia; Liu, Jason; Tseu, Irene; Wang, Jinxia; Kuliszewski, Maciej; Tanswell, A. Keith
CORPORATE SOURCE: (1) Med. Res. Council Group Lung Dev., Neonatal Res. Div., Dep. Pediatr., Hosp. Sick Child. Res. Inst., Univ. Toronto, Toronto, ON Canada
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3107-3115.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Lung branching morphogenesis depends on mesenchymal epithelial tissue interactions. Keratinocyte growth factor (KGF) has been implicated to be a regulator of these tissue interactions. In the present study, we investigated the role of KGF in early rat lung organogenesis. Reverse transcriptase-polymerase chain reaction analysis revealed KGF mRNA expression in the mesenchymal component of the 13-day embryonic lung, while message for KGF receptor (KGFR) was expressed in the epithelium, confirming the paracrine nature of KGF/KGFR axis. **Antisense** KGF oligonucleotides inhibited DNA synthesis of embryonic lung explants. This inhibitory effect of **antisense** KGF was partially reversed by the addition of exogenous KGF. Recombinant KGF was mitogenic for 13-day isolated embryonic lung epithelial cells. Medium conditioned by 13-day lung mesenchymal cells also stimulated DNA synthesis of 13-day embryonic lung epithelial cells. This stimulatory effect was partially abrogated by a neutralizing KGF antibody. The number of terminal buds of lung explants cultured in the presence of **antisense** KGF oligonucleotides was significantly reduced compared to control explants. Exogenous KGF partially abrogated the inhibitory effect of **antisense** KGF on early lung branching. Sense or scrambled KGF oligonucleotides had no inhibitory effect on lung growth and branching. Addition of neutralizing KGF antibodies to the explants also reduced the degree of branching, while non-immune IgG and neutralizing acidic FGF antibodies had no effect. Explants incubated with **antisense** oligonucleotides targeted to the initiation site of translation of both the splice variants of the fibroblast growth factor receptor-2 (**FGFR2**) gene, KGFR and bek, exhibited a similar reduction in lung branching as observed with **antisense** KGF oligonucleotides. **Antisense** KGFR-specific oligonucleotides dramatically inhibited lung branching, while exposure of explants to **antisense** bek-specific oligonucleotides resulted in reduced branching albeit to a lesser degree than that observed with **antisense** KGFR-specific oligonucleotides. Neither sense nor scrambled KGFR-specific oligonucleotides had any effect on early lung branching. These results suggest that the KGF/KGFR system has a critical role in early lung organogenesis.

L51 ANSWER 4 OF 9 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95054295 MEDLINE

DOCUMENT NUMBER: 95054295 PubMed ID: 7964981
TITLE: Basic fibroblast growth factor and fibroblast growth factor receptor I are implicated in the growth of human astrocytomas.
AUTHOR: Morrison R S; Yamaguchi F; Saya H; Bruner J M; Yahanda A M; Donehower L A; Berger M
CORPORATE SOURCE: Department of Neurosurgery, University of Texas M.D. Anderson Cancer Center, Houston 77030.
SOURCE: JOURNAL OF NEURO-ONCOLOGY, (1994) 18 (3) 207-16. Ref: 74
Journal code: 8309335. ISSN: 0167-594X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941128

AB Malignant astrocytomas are highly invasive, vascular neoplasms that comprise the majority of nervous system tumors in humans. A strong association has previously been made between malignancy in human astrocytic tumors and increased expression of certain fibroblast growth factor (FGF) family members, including basic and acidic FGF. The influence of endogenous basic FGF on glioblastoma cell growth in vitro was evaluated using basic FGF-specific **antisense** oligonucleotides. These studies indicated that human glioblastoma cell growth in vitro, can be inhibited by suppressing basic FGF expression. Human astrocytomas also exhibited changes in FGF receptor (FGFR) expression during the course of their progression from a benign to a malignant phenotype. **FGFR2** (bek) expression was abundant in normal white matter and in all low grade astrocytomas, but was not observed in glioblastomas. Conversely, FGFR1 (flg) expression was absent or barely detectable in normal white matter, but was significantly elevated in glioblastomas. Glioblastomas also expressed an alternatively spliced form of FGFR1 containing two immunoglobulin-like disulfide loops (FGFR1 beta), whereas normal human adult and fetal brain expressed a form of the receptor containing three immunoglobulin-like disulfide loops (FGFR1 alpha). Intermediate grades of astrocytic tumors exhibited a gradual loss of **FGFR2** and a shift in expression from FGFR1 alpha to FGFR1 beta as they progressed from a benign to a malignant phenotype. The underlying cytogenetic changes that contribute to these alterations are not entirely understood, but abnormalities in the p53 tumor suppressor gene may influence expression of bFGF as well as the FGFR. These results suggest that alterations in FGFR signal transduction pathways may play a critical role in the malignant progression of astrocytic tumors.

L51 ANSWER 5 OF 9 MEDLINE
ACCESSION NUMBER: 2002461850 IN-PROCESS
DOCUMENT NUMBER: 22209201 PubMed ID: 12221006
TITLE: Ectodermal FGFs Induce Perinodular Inhibition of Limb Chondrogenesis in Vitro and in Vivo via FGF Receptor 2.
AUTHOR: Moftah Marie; Downie Sherry; Bronstein Natalie; Mezentseva Nadezhda; Pu Jiayu; Maher Pamela; Newman Stuart
SOURCE: DEVELOPMENTAL BIOLOGY, (2002 Sep 15) 249 (2) 270.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020911
Last Updated on STN: 20020911

AB The formation of cartilage elements in the developing vertebrate limb,

where they serve as primordia for the appendicular skeleton, is preceded by the appearance of discrete cellular condensations. Control of the size and spacing of these condensations is a key aspect of skeletal pattern formation. Limb bud cell cultures grown in the absence of ectoderm formed continuous sheet-like masses of cartilage. With the inclusion of ectoderm, these cultures produced one or more cartilage nodules surrounded by zones of noncartilaginous mesenchyme. Ectodermal fibroblast growth factors (FGF2 and FGF8), but not a mesodermal FGF (FGF7), substituted for ectoderm in inhibiting chondrogenic gene expression, with some combinations of the two ectodermal factors leading to well-spaced cartilage nodules of relatively uniform size. Treatment of cultures with SU5402, an inhibitor FGF receptor tyrosine kinase activity, rendered FGFs ineffective in inducing perinodular inhibition. Inhibition of production of FGF receptor 2 (**FGFR2**) by transfection of wing and leg cell cultures with **antisense** oligodeoxynucleotides blocked appearance of ectoderm- or FGF-induced zones of perinodular inhibition of chondrogenesis and, when introduced into the limb buds of developing embryos, led to shorter, thicker, and fused cartilage elements. Because **FGFR2** is expressed mainly at sites of precartilage condensation during limb development in vivo and in vitro, these results suggest that activation of **FGFR2** by FGFs during development elicits a lateral inhibitor of chondrogenesis that limits the expansion of developing skeletal elements.

L51 ANSWER 6 OF 9 MEDLINE
ACCESSION NUMBER: 1999429831 MEDLINE
DOCUMENT NUMBER: 99429831 PubMed ID: 10498824
TITLE: Suppression of glioblastoma cell growth following **antisense** oligonucleotide-mediated inhibition of fibroblast growth factor receptor expression.
AUTHOR: Yamada S M; Yamaguchi F; Brown R; Berger M S; Morrison R S
CORPORATE SOURCE: Department of Neurosurgery, Nippon Medical School, Tokyo, Japan.
CONTRACT NUMBER: NS31775 (NINDS)
SOURCE: GLIA, (1999 Oct) 28 (1) 66-76.
Journal code: 8806785. ISSN: 0894-1491.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991122

AB Astrocytes exhibit significant changes in fibroblast growth factor receptor (FGFR) gene expression during malignant progression. These changes include induction of FGFR1 and concomitant loss of **FGFR2** expression. The induction of FGFR1 is believed to endow malignant astrocytes with a selective growth advantage. Glioblastoma (the most malignant form of astrocytoma) cell lines, which exhibit the same pattern of FGFR gene expression as glioblastoma biopsies, were used to evaluate the contribution of FGFR1 expression to glioblastoma cell growth. Addition of phosphorothioate-modified **antisense** oligonucleotides complementary to the initiation site or the alpha exon of the FGFR1 gene suppressed growth of human glioblastoma-derived cell lines. Reverse **antisense** controls or **antisense** oligonucleotide complementary to **FGFR2** had no effect on proliferation. Consistent with its growth-suppressive effect, FGFR1 **antisense** oligonucleotides markedly reduced expression of both FGFR1 mRNA and high-affinity bFGF binding sites, whereas FGFR1 reverse **antisense** control oligonucleotide had no effect. **Antisense** oligonucleotide targeted to the alpha exon of the FGFR1 gene suppressed alpha and beta alternatively spliced FGFR1 mRNA isoforms but did not alter the expression of related FGFR family members. Fluorescein-labeled **antisense** and reverse control oligonucleotides demonstrated cellular uptake and

nuclear accumulation. These results indicate that alterations in FGFR expression may contribute to malignant proliferation in human astrocytomas. These findings also illustrate the high degree of selectivity that can be obtained with **antisense** oligonucleotides, a property that is essential for employing these reagents therapeutically.

L51 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:661781 CAPLUS
TITLE: Ectodermal FGFs Induce Perinodular Inhibition of Limb Chondrogenesis in Vitro and in Vivo via FGF Receptor 2
AUTHOR(S): Moftah, Marie Z.; Downie, Sherry A.; Bronstein, Natalie B.; Mezentseva, Nadezhda; Pu, Jiayu; Maher, Pamela A.; Newman, Stuart A.
CORPORATE SOURCE: Department of Cell Biology and Anatomy, New York Medical College, Valhalla, NY, 10595, USA
SOURCE: Developmental Biology (Orlando, FL, United States) (2002), 249(2), 270-282
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of cartilage elements in the developing vertebrate limb, where they serve as primordia for the appendicular skeleton, is preceded by the appearance of discrete cellular condensations. Control of the size and spacing of these condensations is a key aspect of skeletal pattern formation. Limb bud cell cultures grown in the absence of ectoderm formed continuous sheet-like masses of cartilage. With the inclusion of ectoderm, these cultures produced one or more cartilage nodules surrounded by zones of noncartilaginous mesenchyme. Ectodermal fibroblast growth factors (FGF2 and FGF8), but not a mesodermal FGF (FGF7), substituted for ectoderm in inhibiting chondrogenic gene expression, with some combinations of the two ectodermal factors leading to well-spaced cartilage nodules of relatively uniform size. Treatment of cultures with SU5402, an inhibitor FGF receptor tyrosine kinase activity, rendered FGFs ineffective in inducing perinodular inhibition. Inhibition of prodn. of FGF receptor 2 (**FGFR2**) by transfection of wing and leg cell cultures with **antisense** oligodeoxynucleotides blocked appearance of ectoderm- or FGF-induced zones of perinodular inhibition of chondrogenesis and, when introduced into the limb buds of developing embryos, led to shorter, thicker, and fused cartilage elements. Because **FGFR2** is expressed mainly at sites of precartilage condensation during limb development in vivo and in vitro, these results suggest that activation of **FGFR2** by FGFs during development elicits a lateral inhibitor of chondrogenesis that limits the expansion of developing skeletal elements.

L51 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:566264 CAPLUS
DOCUMENT NUMBER: 131:167361
TITLE: Cellular arrays for rapid molecular profiling
INVENTOR(S): Kallioniemi, Olli; Kononen, Juha; Leighton, Stephen B.; Sauter, Guido
PATENT ASSIGNEE(S): The United States of America as Represented by the Secretary Department of Health, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9944062	A1	19990902	WO 1999-US4000	19990224
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2318789	AA	19990902	CA 1999-2318789	19990224
AU 9929735	A1	19990915	AU 1999-29735	19990224
EP 1066517	A1	20010110	EP 1999-910986	19990224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002505431	T2	20020219	JP 2000-533759	19990224
US 2002132246	A1	20020919	US 2001-971742	20011004
PRIORITY APPLN. INFO.:			US 1998-75979P P	19980225
			US 1998-106038P P	19981028
			WO 1999-US4000 W	19990224
			US 1999-150493P P	19990824
			US 1999-429448 B1	19991028

AB A method is disclosed for rapid mol. profiling of tissue or other cellular specimens by placing a donor specimen in an assigned location in a recipient array, providing copies of the array, and performing a different biol. anal. of each copy. In one embodiment, the copies of the array are formed by placing elongated specimens in a three dimensional matrix, and cutting sections from the matrix to form multiple copies of a two dimensional array that can then be subjected to the different biol. analyses. Alternatively, the array can be formed from cell suspensions such that identical multiple copies of an array are formed, in which corresponding positions in the copies of the array have samples from the same or similar specimen. The results of the different biol. analyses are compared to det. if there are correlations between the results of the different biol. analyses at each assigned location. In some embodiments, the specimens may be tissue specimens from different tumors, which are subjected to multiple parallel mol. (including genetic and immunol.) analyses. The results of the parallel analyses are then used to detect common mol. characteristics of the tumor type, which can subsequently be used in the diagnosis or treatment of the disease. The biol. characteristics of the tissue can be correlated with clin. or other information, to detect characteristics assocd. with the tissue, such as susceptibility or resistance to particular types of drug treatment. Other examples of suitable tissues which can be placed in the matrix include tissue from transgenic or model organisms, or cellular suspensions (such as cytol. prepns. or specimens of liq. malignancies or cell lines).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1996:554952 CAPLUS
DOCUMENT NUMBER:	125:185871
TITLE:	**Antisense** oligonucleotides for treating glioblastoma cells
INVENTOR(S):	Morrison, Richard S.; Tseng, Ben Y.; Brown, Bob D.
PATENT ASSIGNEE(S):	Genta Incorporated, USA
SOURCE:	PCT Int. Appl., 71 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621471	A1	19960718	WO 1996-US331	19960111
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5783683	A	19980721	US 1995-371001	19950110
CA 2209989	AA	19960718	CA 1996-2209989	19960111
AU 9646552	A1	19960731	AU 1996-46552	19960111
EP 871494	A1	19981021	EP 1996-902124	19960111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10512446	T2	19981202	JP 1996-521791	19960111

PRIORITY APPLN. INFO.: US 1995-371001 19950110
WO 1996-US331 19960111

AB **Antisense** oligonucleotides which bind to pre-mRNA expressed by human FGF receptor gene 1 (FGFR1) are incorporated into vectors to suppress the growth of human glioma and glioblastoma cells. Preferred oligonucleotides include phosphorothioate analogs and bind to the .alpha.-exon pre-mRNA. Thus, the phosphorothioate analog of the .alpha.-exon-specific oligonucleotide CTGCACATCGTCCCGCAGCC inhibited the growth of human glioblastoma cells in vitro by 70-80% at 30 .mu.M and reduced the expression of FGFR1 mRNA without affecting the expression of **FGFR2** mRNA.